Physiopathology and diagnosis of nephrogenic diabetes insipidus

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Abstract: Nephrogenic diabetes insipidus (NDI) is caused by an improper response of the kidney to the antidiuretic hormone arginine vasopressin (AVP), leading to a decreased ability to concentrate urine which results in polyuria and polydipsia. The clinical diagnosis of NDI relies on demonstration of subnormal ability to concentrate urine despite the presence of AVP. NDI is most commonly acquired, secondary to kidney disorders, electrolyte imbalance and various drugs. Congenital forms of NDI are rare, and most commonly inherited in a X-linked manner with mutations of the AVP receptor type 2 (AVPR2). Mutations of the water channel aquaporin-2 (AQP2) can be detected in autosomal recessive or dominant forms of NDI. Management of NDI should focus on free access to drinking water and reduction of polyuria. = Le diabète insipide néphrogénique (DIN) est causé par une réponse inappropriée du rein à l'hormone antidiurétique (ADH), entraînant une diminution de la capacité de concentrer l'urine, se manifestant par l'association polyurie et polydipsie. Le diagnostic clinique de DIN repose sur la démonstration du défaut de concentration de l'urine malgré la présence d'ADH. Le DIN est le plus souvent acquis, suite à diverses maladies rénales, troubles ioniques, ou médicaments. Les formes congénitales de DIN sont rares, le plus souvent liées au chromosome X en relation avec des mutations du récepteur de l'ADH de type 2 (gène AVPR2). Des mutations du gène AQP2 codant pour le canal à eau aquaporine-2 sont retrouvées dans les formes transmises sur un mode dominant ou récessif. Le traitement du DIN vise à maintenir l'accès à l'eau potable et à réduire la polyurie.

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Physiopathology and Diagnostic of Nephrogenic Diabetes Insipidus

Physiopathologie et diagnostic du diabète insipide néphrogénique

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Nephrogenic diabetes insipidus (NDI) is caused by an improper response of the kidney to the antidiuretic hormone arginine vasopressin (AVP), leading to a decrease in the ability to concentrate urine by removing free water in the distal nephron. This results in polyuria (excessive urine production, which can reach up to 10L a day in children) and polydipsia (excessive thirst). Infants affected by the inherited forms of the disease usually show failure to thrive, fever, constipation, and episodes of severe hypernatremic dehydration with risk of neurological sequels. Short stature and secondary dilatation of the ureters and bladder from the high urine volume is common (1,2).

The clinical diagnosis of NDI relies on demonstration of subnormal ability to concentrate urine despite the presence of AVP. Differential diagnosis includes neurogenic/central diabetes insipidus (lack of AVP), psychogenic polydipsia (compulsive water drinking) and diabetes mellitus (polyuria due to glucosuria). The diagnosis relies on the simultaneous measurement of sodium concentration (or osmolality) in plasma and urine: increased plasma sodium (> 145 mEq/L) or osmolality (> 290 mOsm/kg) in the presence of diluted urine is suggestive of NDI. The differential diagnosis can also be made by using the water deprivation test and/or administration of DDAVP (desmopressin) intranasally. If the patient is able to concentrate urine following administration of DDAVP, then the cause of the diabetes insipidus is neurogenic; if no response occurs to DDAVP administration, then the cause is likely to be nephrogenic (1,2).

NDI is most commonly acquired, secondary to kidney disorders such as polycystic kidney disease, amyloidosis, sickle cell disease, granulomatous diseases, chronic infection, urinary tract obstruction, Sjögren syndrome, vascular disorders, electrolyte imbalance (hypokalemia, hypercalcemia) and various drugs (lithium, amphotericin B, orlistat, ifosfomide, ofloxacin, cidofovir, vaptans, etc...) (3). Congenital forms of NDI are rare, with a prevalence estimated at 1-2/1 000 000. Congenital NDI is most commonly inherited in a X-linked manner (~90% of individuals), in relation with mutations of the AVP receptor type 2 (*AVPR2*). NDI can also be inherited in an autosomal recessive manner (~9% of individuals) or in an autosomal dominant manner (~1% of individuals), in relation with muations of the water channel aquaporin-2 (*AQP2*). Molecular genetic testing of the two genes associated with NDI (*AQP2* and *AVPR2*) is clinically available (2,4,5).

Management of NDI should focus on free access to drinking water and reduction of polyuria by using thiazide diuretics and/or potassium-sparing diuretic (amiloride), dietary restriction of sodium, and nonsteroidal anti-inflammatory drugs (NSAIDs). Patients with congenital NDI should be monitored for growth, serum sodium concentration and hydration status, and development of hydronephrosis (renal ultrasound).

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Abstract

Nephrogenic diabetes insipidus (NDI) is caused by an improper response of the kidney to the antidiuretic hormone arginine vasopressin (AVP), leading to a decreased ability to concentrate urine which results in polyuria and polydipsia. The clinical diagnosis of NDI relies on demonstration of subnormal ability to concentrate urine despite the presence of AVP. NDI is most commonly acquired, secondary to kidney disorders, electrolyte imbalance and various drugs. Congenital forms of NDI are rare, and most commonly inherited in a X-linked manner with mutations of the AVP receptor type 2 (*AVPR2*). Mutations of the water channel aquaporin-2 (*AQP2*) can be detected in autosomal recessive or dominant forms of NDI. Management of NDI should focus on free access to drinking water and reduction of polyuria.

Key-words: arginine vasopressin, V2 receptor, urinary concentration, aquaporin-2

Résumé

Le diabète insipide néphrogénique (DIN) est causé par une réponse inappropriée du rein à l'hormone antidiurétique (ADH), entraînant une diminution de la capacité de concentrer l'urine, se manifestant par l'association polyurie et polydipsie. Le diagnostic clinique de DIN repose sur la démonstration du défaut de concentration de l'urine malgré la présence d'ADH. Le DIN est le plus souvent acquis, suite à diverses maladies rénales, troubles ioniques, ou médicaments. Les formes congénitales de DIN sont rares, le plus souvent liées au chromosome X en relation avec des mutations du récepteur de l'ADH de type 2 (gène *AVPR2*). Des mutations du gène *AQP2* codant pour le canal à eau aquaporine-2 sont retrouvées dans les formes transmises sur un mode dominant ou récessif. Le traitement du DIN vise à maintenir l'accès à l'eau potable et à réduire la polyurie.

Mots-clés: hormone antidiurétique, récepteur V2, concentration de l'urine, aquaporine-2